UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/806,930	03/22/2004	Sergey Anatolievich Lukyanov	CLON-094	2888

24353 7590 01/27/2006

BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
MONDESI, ROBERT B	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 01/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/806,930	LUKYANOV, SERGEY ANATOLIEVICH	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 16-26* is/are pending in the application.

4a) Of the above claim(s) *16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 17-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 25, 2005 has been entered.

Status of the claim(s)

Claims 11-15 have been canceled. **Claims 1-10 and 17-26** are pending and presently under examination. On Page 1, line 11 of the remarks in amendment filed on August 25, 2005 applicants have indicated that **claim 16** has been canceled as being directed to withdrawn subject matter, but the claim status identifier in the claim sheets states that the claim is withdrawn. The examiner acknowledges applicants' intent and has noted the inconsistencies; however the claim is being treat as a withdrawn claim.

Information Disclosure Statement

The IDS filed January 24, 2005 has been received and is signed and considered, a copy of the PTO 1449 is attached to the following document.

Claim of Benefit

Applicants' arguments in regards to claim of benefit to provisional applications No. 60/356,225 filed February 11, 2002 and No. 60/383,336 filed May 22, 2002 have

been found persuasive; however applicants' arguments in regards to claim of benefit to non-provisional application No. 09/976,673 filed October 12, 2001 have not been found persuasive.

Applicants assert that non-provisional application No. 09/976,673 provides on page 40, lines 18-23 and figures 12 and 13, a working example describing a nucleic acid encoding the polypeptide Cr-44-9. The applicants assert further that "the Cr-44-9 polypeptide comprises a first and a second chromo/fluorescent domain as required by Claim 1 of the present application and moreover, as noted on page 19, lines 17 to 23, the chromo-fluorescent domains are derived from *Heteractis crispa*, which is a *Cnidarian* species".

As mentioned above applicants' arguments have not been found persuasive. First and foremost the specification for non-provisional application No. 09/976,673 only contains 36 pages; therefore there is no page 40 for the examiner to refer to. Presently the description for figures 12 and 13, in the Brief Description of Drawings, merely states that "Figure 12/13 provides the amino acid and encoding nucleotide sequence for the Cr-449 tandem fusion protein", and there is no mention of the claimed invention which is a nucleic acid encoding a polypeptide product comprising a first chromo/fluorescent domain and a second chromo/fluorescent domain, wherein said first and second chromo/fluorescent domains oligomerize under intracellular conditions so that said encoded polypeptide assumes a tertiary structure. In fact nowhere in the non-provisional application No. 09/976,673 is a description that is supportive of the claimed subject matter and satisfies the requirements of written description under 35 U.S.C 112,

first paragraph. In the specification of application No. 09/976,673, there is no mention of a nucleic acid product that encodes a polypeptide which has a first and second fluorescent domain that oligomerize under intracellular conditions. The only reference to any oligomerization-taking place is on page 9, lines 15-20 wherein it is stated, "of particular interest are oligomerization mutants that do not oligomerize under intracellular conditions".

Also, note to the applicants, *Heteractis crispa* is a species of the family *Stichodactylidae*, which is discussed and has support in the non-provisional application No. 09/976,673; however claims 3-5 and 19-21 are drawn to *Cnidarian* and *Anthozoan* species which are much broader taxonomy classifications and include many more species. For instance *Cnidarian* is a phylum, which contains many classes such as *Hydrozoan* and *Anthozoan*. The class of *Anthozoan* contains several sub classes that themselves contain a variety of orders. The order of *Scleractinia*, which resides in the subclass of *Hexacorallia* and contained in the Class of *Anthozoan*, contains 256 species - one of which would be comparable in classification to *Heteractis crispa*.

Therefore *Heteractis crispa* is of a very narrow scope and does not provide support for the extensively broad scope of a phylum such as *Cnidarian*.

When applicant files a continuation-in-part whose claims are not supported by the parent application, the effective filing date is the filing date of the child CIP. Any prior art disclosing the invention or an obvious variant thereof having a critical reference date more than 1 year prior to the filing date of the child will bar the issuance of a patent under 35 U.S.C. 102 (b). *Paperless*

Accounting v. Bay Area Rapid Transit System, 804 F.2d 659, 665, 231 USPQ 649, 653 (Fed. Cir. 1986).

Withdrawal of Objections and Rejections

The objections and rejections not explicitly restated below are withdrawn.

New Objection(s) and Rejection(s)

Specification

This application contains sequence disclosures at page 39, line 31 (amino acid linker RSPG) and Figure 6A (amino acid linker RSPG and RTRA) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a((1) and (a)(2). However, this application fails to comply with one or more of the requirements of 37 C.F.R. § 1.821 through 1.825 for one or more of the reasons set forth on the attached form "Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequences And/Or Amino Acid Sequence Disclosures". Wherein attention is directed to paragraph(s) §1.82 (c) and (e). Although an examination of this application on the merits can proceed without prior compliance, compliance with the Sequence Rules is required for the response to this Office action to be complete. Examiner would like to point out that there is no information with regards to SEQ ID NO:s of the mentioned amino acid linkers (amino acid linker RSPG and RTRA) in the Brief Description of the Drawings for Figure 6A. If the Drawings contain amino acid sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a((1) and (a)(2) then the Brief Description of the Drawings needs to state the SEQ ID NO:s for the nucleotide and/or

amino acid sequences. Unless the appropriate SEQ ID NO:s accompany the nucleotide and/or amino acid sequences in the actual Drawing sheet.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 and 17-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids (SEQ ID NO:s 3, 5, 7 and 9) encoding tandem chromo/fluorescent polypeptides Cr-44-9 tandem (SEQ ID NO: 4) HcRed2A tandem (SEQ ID NO: 6), M355NA tandem (SEQ ID NO:8), DsRed2-tandem (SEQ ID NO: 10) does not reasonably provide enablement for all nucleic acids encoding polypeptide products comprising a first chromo/fluorescent domain and second chromo/fluorescent domain, wherein said first and second chromo/fluorescent domains are oilgomeric and oilgomerize under intracellular conditions so that the said polypeptide assumes a tertiary structure; including nucleic acids that encode polypeptides wherein the first and second chromo/fluorescent domains are chromo/fluorescent domains from *Cnidarian* or *Anthozoan* species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir.1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a

correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In Wands, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (Wands, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of Wands factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1-2.Breadth of the claims and the nature of the invention.

The invention is a nucleic acid encoding a polypeptide product comprising a first chromo/fluorescent domain and second chromo/fluorescent domain, wherein said first and second chromo/fluorescent domains are oilgomeric and oilgomerize under intracellular conditions so that the said polypeptide assumes a tertiary structure. The invention includes nucleic acids that encode polypeptides wherein the mentioned first and second chromo/fluorescent domains are chromo/fluorescent domains from *Cnidarian* or *Anthozoan* species. The invention also encompasses a construct comprising a vector and the said nucleic acid; an expression cassette comprising a transcriptional initiation region functional in an expression host and the said nucleic acid; a cell or progeny comprising the said expression cassette; and a method of

producing the said polypeptide product. It is important to indicate that the breadth and scope of the invention is so broad that it includes any nucleic acid encoding a tandem polypeptide product wherein the polypeptide comprises first and second chromo/fluorescent domains that oligomerize under intracellular conditions.

3. The state of prior art.

The prior art does not disclose nucleic acids that encode polypeptide products that comprise oligomeric chromo/fluorescent domains that oligomerize under intercellular conditions so that the encoded polypeptide assumes a tertiary structure- regardless of what species the chromo/fluorescent domains are derived from. The concept of oilgomeric interactions is reserved for monomers such as peptides or polypeptide subunits that undergo dimerization or trimerization. The prior art is silent with regards to fluorescent polypeptides comprising linked tandem domains that undergo oligomerization, as this would not be in accordance with the art recognized definition of oligomerization (see Baird et al., 2000 and Answers.com publication cited in PTO-892; also, for further clarification and explanation see rejection of claims under 35 U.S.C. 112, second paragraph stated below).

However the prior art discloses a nucleic acid that encodes a polypeptide product that comprises a first and second chromo/fluorescent domain wherein the said chromo/fluorescent domains are form a non-bioluminescent *Anthozoan* species.

Fradkov et al. teach that a novel gene for the advanced red shifted protein with an emission maximum at 593 nm was cloned from *Discosoma* (phylum *Cnidarian*, class *Anthozoan*) coral. The mentioned protein dsFP593 is highly homologous to the recently

described GFP-like protein drFP583 with an emission maximum at 583 nm and using the similarity of the drFP583 and dsFP593 genes a "scuffling" procedure was performed to generate a pool of mutants consisting of various combinations of parts of both genes; one "hybrid gene" was chosen for the subsequent random mutagenesis, which resulted in a mutant variant with a uniquely red-shifted emission maximum at 616nm (Abstract, page 127, lines 1-11).

4. The relative skill in the art.

That of a M.D. or Ph. D. level individual as it relates to the product of the invention characterizes the relative skill in the art.

5. The level of predictability in the art.

The level of predictability in the art and the amount of guidance present is low with regards to the product of the invention. As mentioned previously the concept of a self oligomerizing tandemly linked monomer comprising a first and second chromo/fluorescent domain wherein the domains oligomerize to contribute to a tertiary structure is not addressed in the prior art. However, the prior art provides various approaches wherein the oilgomerization of fluorescent monomers or protein subunits that are not linked can be studied. For instance Baird et al., 2000, discuss the oligomerization of DsRed, a red fluorescent protein from coral, expressed via a yeast two-hybrid system wherein two separate DsRed domains are expressed using fusions to both the Gal4 DNA binding domain and the Gal4 activation domain in HFC yeast. In view of applicants claimed invention, and the methods disclosed in the prior art, such as the one exemplified by Baird et al., 2000, it is difficult for a person skill in the art to

predict that all tandemly linked chromo/fluorescent domains will oligomerize under intracellular conditions.

6. The amount of guidance present.

The guidance that the applicants have provided only pertains to the specific species; nucleic acids (SEQ ID NO:s 3, 5, 7 and 9) encoding tandem chromo/fluorescent polypeptides Cr-44-9 tandem (SEQ ID NO: 4) HcRed2A tandem (SEQ ID NO: 6), M355NA tandem (SEQ ID NO:8), DsRed2-tandem (SEQ ID NO:10) that have been described in the specification of the present application. The applicants have not described a sufficient number of species in order to provide guidance for the entire scope of the claimed nucleic acids. In order for a person skill in the art to know that two linked chromo/fluorescent domains will oilgomerize under intracellular conditions, as the applicants have claimed, a disclosure of the domains themselves would be required since not all chromo/fluorescent domains interact to form dimers or trimers.

7. The existence of working examples.

On pages 37-42 of the specification of the present application, the applicants have provided the following working examples: nucleic acids (SEQ ID NO:s 3, 5, 7 and 9) encoding tandem chromo/fluorescent polypeptides Cr-44-9 tandem (SEQ ID NO: 4) HcRed2A tandem (SEQ ID NO: 6), M355NA tandem (SEQ ID NO:8), DsRed2-tandem (SEQ ID NO:10) and fusion proteins comprising the mentioned polypeptides.

8. The quantity of experimentation necessary.

The amount of experimentation that is required is undue: while the applicants have disclosed a certain number of species of the claimed nucleic acid of the invention (four to be exact) that would encode a polypeptide comprising a first and second chromo/fluorescent domain that oligomerize under intracellular conditions. It would not be routine, without a knowledge of the specific chromo/fluorescent domain and further analysis, for a person skill in the art to know that all nucleic acids encoding polypeptides with a first and second chromo/fluorescent domain will encode polypeptides that have oligomerizing first and second chromo/fluorescent domains; therefore this in effect creates a requirement for more experimentation. In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention.

It must be noted that the issue in this case is the breath of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The Applicants make and test position is inconsistent with the decisions of *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) where it is stated that "... scope of claims must bear a reasonable correlation to scope of enablement provided by the specification to persons of ordinary skill in the art...". Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive

and undue. See *In re Wands*, 858 F.2d at 737, 8 USPQZd at 1404 (Fed. Cir. 1988). Therefore, for the instant specification to be enabling, it needs to provide direction/guidance regarding an acceptable number of different nucleic acids encoding polypeptides comprising the mentioned domains.

Absent sufficient guidance/direction one of skill in the art would not be able to practice the claimed invention commensurate in scope with the claims. Thus, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention as the amount of experimentation required is undue, due to the broad scope of the claims, the lack of guidance and insufficient working examples provided in the specification and the high degree of unpredictability as evidenced by the state of the prior art, attempting to test all the different types of nucleic acids encompassed by the claimed invention would constitute undue experimentation. Therefore, applicants have not provided sufficient guidance to enable one of skill in the art to make and use the claimed invention in a manner that reasonably correlates with the scope of the claims, to be considered enabling.

Claims 1-10 and 17-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In **claims 1-2 and 17** the applicants state that the nucleic acid of the invention encodes a single polypeptide product that comprises two separate chromo/fluorescent domains that oligomerize in order to assume a tertiary structure and also that the first and second chromo/fluorescent domains are oligomeric producing domains. The

mentioned claim language fails to make sense to a person skill in the art and is repugnant to the accepted understating of oligomerization of peptides and tertiary structure in the art. Oilgomerization is a phenomenon that is defined to occur between two or more peptides or polypeptide subunits (monomers). For instance Baird et al., 2000, discuss the oligomerization of DsRed, a red fluorescent protein from coral, expressed via a yeast two-hybrid system wherein two separate DsRed domains are expressed using fusions to both the Gal4 DNA binding domain and the Gal4 activation domain in HFC yeast (Page 11988, column 1, paragraph 3, lines1-15). In biochemistry oligomerization occurs between two or more subunits to form a protein complex (see Answers.com publication cited in PTO-892). These mentioned subunits are peptides (monomers) that already have a tertiary structure and they are not domains that help form the tertiary structure of a given peptide. So it is not clear as to how the applicants envision the domains of a peptide to oilgomerize in order to form a protein complex, which assumes a particular tertiary structure.

Claims 3-10 and 18-26 are dependent claims that do not remedy the deficiencies of the independent claim that they depend therefrom.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 7-10, 17-21 and 23-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Fradkov et al., 2000 (Cited in IDS filed June 23, 2004) as evidenced by Matz et al., 1999 (Cited in IDS filed June 23, 2004).

The invention is a nucleic acid encoding a polypeptide product comprising a first chromo/fluorescent domain and second chromo/fluorescent domain, wherein said first and second chromo/fluorescent domains are oilgomeric and oilgomerize under intracellular conditions so that the said polypeptide assumes a tertiary structure. The invention includes nucleic acids that encode polypeptides wherein the mentioned first and second chromo/fluorescent domains are chromo/fluorescent domains from *Cnidarian* or *Anthozoan* species. The invention also encompasses a construct comprising a vector and the said nucleic acid; an expression cassette comprising a transcriptional initiation region functional in an expression host and the said nucleic acid; a cell or progeny comprising the said expression cassette; and a method of producing the said polypeptide product.

Fradkov et al. teach that a novel gene for the advanced red shifted protein with an emission maximum at 593 nm was cloned from *Discosoma* (phylum *Cnidarian*, class *Anthozoan*) coral. The mentioned protein dsFP593 is highly homologous to the recently described GFP-like protein drFP583 with an emission maximum at 583 nm and using the similarity of the drFP583 and dsFP593 genes a "scuffling" procedure was performed to generate a pool of mutants consisting of various combinations of parts of both genes; one "hybrid gene" was chosen for the subsequent random mutagenesis, which resulted

in a mutant variant with a uniquely red-shifted emission maximum at 616nm (Abstract, page 127, lines 1-11).

Fradkov et al. teach further that the ds/dr hybrid clone contains the larger N-terminal part (residues 1-180) of the dsFP503 gene and the smaller C-terminal part (from residue 181 to IV (3') end) of the drFP583 gene (Page 129, column 2, paragraph, 3, lines 1-3 and Fig. 3, page 130)

Fradkov et al. teach that the new gene, dsFP593 is isolated from a non-bioluminescent *Discosoma* species (phylum *Cnidarian*, class *Anthozoan*) and as evidenced by Matz et al., 1999, drFP583 is also isolated from a non-bioluminescent Discosoma species (phylum *Cnidarian*, class *Anthozoan*) commonly known as DsRed (Page 971, table 2).

Fradkov et al. teach further that cDNA fragments encoding the drFP583 and dsFP593 proteins were amplified using PCR conditions using four specific primers. The PCR product (~ 700 bp) was digested and sub-cloned into the pQE-30 vector and after random mutagenesis the vector containing the ds/dr-hybrid gene was used to transform DH5alpha cells (Page 127, column 1, paragraph 3, lines 1-13; paragraph 5, lines 1-5).

Fradkov et al. teach that for protein expression, cells carrying the recombinant plasmid were grown in LB and protein was the expressed protein was purified using Talon Metal Affinity Resin (Page 128, column 1, paragraph 1, lines 1-7).

With regards to the functional limitations of the claims presented by the applicants that the nucleic acid of the invention encodes a polypeptide product comprising a first chromo/fluorescent domain and second chromo/fluorescent domain,

wherein said first and second chromo/fluorescent domains are oilgomeric and oilgomerize under intracellular conditions so that the said polypeptide assumes a tertiary structure, it is of importance to note that, "Products of identical chemical composition can not have mutually exclusive properties." A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Thus Fradkov et al., 2000 as evidenced by Matz et al., 1999 teach all the elements of **claims 1-5, 7-10, 17-21 and 23-26** and these claims are anticipated under 35 USC 102(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 18 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fradkov et al., 2000 (Cited in IDS filed June 23, 2004) as evidenced by Matz et al., 1999 (Cited in IDS filed June 23, 2004) in view of WO 01/27150.

Fradkov et al. teach a nucleic acid encoding polypeptide comprising a first and second chromo/fluorescent domains as mentioned above.

Fradkov et al., do not teach that the nucleic acid of the invention encodes a fusion protein of mentioned first and second chromo/fluorescent domains fused to a non-chromo/fluorescent protein domain.

WO 01/27150 teaches a nucleic acid encoding a fusion protein comprising a chromo/fluorescent domain fused to a non-chromo/fluorescent protein domain (Page 9 lines 26-34).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to fuse a non-chromo/fluorescent protein domain to a protein comprising a chromo/fluorescent domain for the advantages of a fusion protein that can bind antibodies specific to the fusion partner, e.g., epitope tags as taught by Fradkov et al., 2000 (as evidenced by Matz et al., 1999) and WO 01/27150, see WO 01/27150 at page 9, lines 29-30.

Conclusion

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert B. Mondesi
Patent Examiner
Group 1653

Robert B
1-22-06

Notice to Comply	Application No.	Applicant(s)	
	10/806,930	LUKYANOV	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The specifcation and the Drawings contain sequences that are not identified by sequence identifiers (see page 39, line 31 and Figure 6A).

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY